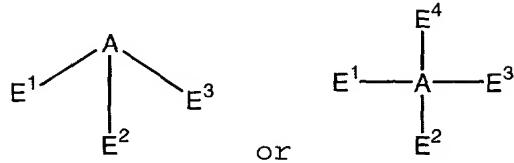


CLAIMS:

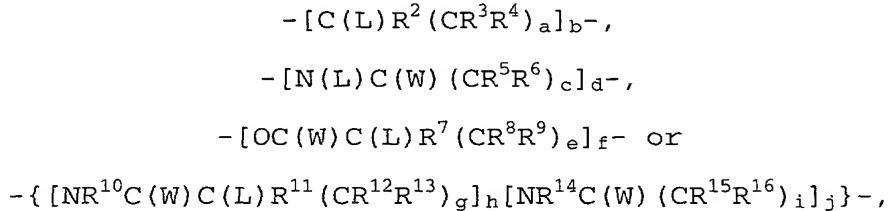
1. A polypodal chelant having the formula:

5



and pharmaceutically acceptable salts thereof, wherein A is a spacer selected from the group consisting of R^1-C , R^1-Si , R^1-Ge , N, P and $P(O)$, or a macrocyclic group
10 having the formula:

15



20

25

wherein a is an integer selected from 1 to 3;
 b is an integer selected from 3 to 5;
 c is an integer selected from 1 to 3;
 d is an integer selected from 3 or 4;
 e is an integer selected from 1 to 3;
 f is an integer selected from 3 or 4;
 g is an integer selected from 1 to 3;
 h is an integer selected from 3 or 4;
 i is an integer selected from 1 to 3;

j is an integer selected from 0 to 3;

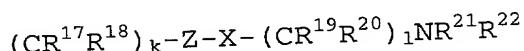
L is a direct bond to E¹, E², E³, and E⁴;

W is H₂ or O;

R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³,

5 R¹⁴, R¹⁵, and R¹⁶ are independently selected at each occurrence from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₁-C₆ fluoroalkyl, C₁-C₆ alkenyl, C₃-C₆ cycloalkenyl, C₁-C₆ fluoroalkenyl, benzyl, fluorobenzyl, phenyl and fluorophenyl;

10 E¹, E², E³, and E⁴ are chelating arms each independently having the formula:



15 wherein k is an integer selected from 0 to 3, provided that when A is N or -[N(L)C(W)(CR⁵R⁶)_c]_d-, k is 1-3;

l is an integer selected from 1 to 3;

Z is selected from the group consisting of a bond,

20 O, NH, NR¹NR¹, ONH and N(OR¹);

X is selected from the group consisting of C(O),

S(O)₂ and P(O)(OR¹);

R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹ and R²² are independently

selected from the group consisting of H, C₁-C₁₀ alkyl substituted with 0-5 R²³, C₁-C₁₀ fluoroalkyl substituted with 0-5 R²³, C₂-C₁₀ alkenyl substituted with 0-5 R²³, C₂-C₁₀ fluoroalkenyl substituted with 0-5 R²³, aryl substituted with 0-5 R²³, C₇-C₁₆ alkaryl wherein the aryl is substituted with 0-5 R²³, and fluoroaryl substituted

30 with 0-5 R²³; or R¹⁷ and R¹⁸, R¹⁹ and R²⁰ or R²¹ and R²² may be taken together to form a C₃-C₁₀ cycloalkyl or C₃-C₁₀ cycloalkenyl optionally interrupted with C(O)NH, NH,

NHC(O), NHC(O)NH, NHC(S)NH, O, S, S(O), S(O)₂, P(O)(OR²⁴), P(O)(OR²⁴)O or P(O)(NHR²⁴)O, or to form a =CH-R^{22a} group, wherein R^{22a} is aryl substituted with 0-5 R²³, or heterocycle substituted by 0-5 R²³;

5 R²³ is selected from the group consisting of H, OH, C₁-C₃ alkyl, C₁-C₃ hydroxyalkyl, C(=O)R²⁴, C(=O)OR²⁴, C(=O)NR²⁴₂, PO(OR²⁴)₂ and S(O)₂OR²⁴; and

10 R²⁴ is selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₁-C₆ fluoroalkyl, C₁-C₆ alkenyl, C₃-C₆ cycloalkyl, C₁-C₆ fluoroalkenyl, benzyl, fluorobenzyl, phenyl, and fluorophenyl.

2. A polypodal chelant according to claim 1, characterized by having four chelating arms.

15

3. A polypodal chelant according to claim 1, characterized by being tripodal.

20 4. A tripodal chelant according to claim 3, wherein A is a spacer selected from the group consisting of R¹-C, N, P, P(O), and -[N(L)C(W)(CR⁵R⁶)_{cl}a-; R¹, R⁵, and R⁶ are selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₁-C₆ alkenyl, C₃-C₆ cycloalkyl, benzyl, and phenyl; E¹, E², and E³ are chelating arms 25 each independently having the formula:



30 R²¹ and R²² are independently selected at each occurrence from the group consisting of H, C₁-C₁₀ alkyl substituted with 0-2 R²³, C₂-C₁₀ alkenyl substituted with 0-2 R²³, aryl substituted with 0-2 R²³, and C₇-C₁₆

alkaryl, wherein the aryl is substituted with 0-2 R²³, or R²¹ and R²² may be taken together to form a =CH-R^{22a} group, wherein R^{22a} is aryl substituted with 0-5 R²³, or heterocycle substituted by 0-5 R²³;

5 R²³ is selected from the group consisting of H, OH, C₁-C₃ alkyl, C₁-C₃ hydroxyalkyl, C(=O)R²⁴, C(=O)OR²⁴, C(=O)NR²⁴₂, PO(OR²⁴)₂ and S(O)₂OR²⁴; and

10 R²⁴ is selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₁-C₆ fluoroalkyl, C₁-C₆ alkenyl, C₃-C₆ cycloalkyl, benzyl and phenyl.

5. A tripodal chelant according to claim 4, wherein A is a spacer selected from the group consisting of N, P(O), and -[N(L)C(W)(CR⁵R⁶)_c]_d-; R⁵ and R⁶ are independently selected at each occurrence from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, phenyl and benzyl; E¹, E², and E³ are chelating arms each independently having the formula:



20

wherein R²¹ and R²² are independently selected from the group consisting of C₁-C₁₀ alkyl substituted with 0-2 R²³, and aryl substituted with 0-2 R²³, or R²¹ and R²² may be taken together to form a =CH-R^{22a} group, wherein R^{22a} is aryl substituted with 0-5 R²³, or heterocycle substituted by 0-5 R²³; R²³ is selected from the group consisting of OH, C₁-C₃ hydroxyalkyl, COOH, PO(OH)₂ and S(O)₂OH.

30 6. A tripodal chelant according to claim 5, wherein A is a spacer selected from the group consisting of N, and P(O); E¹, E² and E³ are chelating arms each independently having the formula:



5 wherein k is 2-3; R²¹ is independently selected from
 the group consisting of CH₃, CH₂COOH, and CH₂PO(OH)₂; and
 R²² is independently selected from the group consisting
 of CH₂COOH, and CH₂PO(OH)₂.

7. A tripodal chelant according to claim 6,
 wherein A is N or P(O); E¹, E², and E³ are (CH₂)_k-
 10 NHCOCH₂N(CH₂COOH)₂, and k is 2-3.

8. A tripodal chelant according to claim 7,
 wherein A is N; E¹, E² and E³ are (CH₂)_k-
 15 NHCOCH₂N(CH₂COOH)₂, and k is 2-3.

9. A tripodal chelant according to claim 7,
 wherein A is N; E¹, E² and E³ are (CH₂)_k-
 20 NHCOCH₂N(CH₃)(CH₂COOH), and k is 2-3.

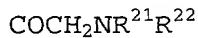
10. A tripodal chelant according to claim 7,
 wherein A is N; E¹, E², and E³ are (CH₂)_k-NHCOCH₂N=CH-R^{22a},
 k is 2-3, and R^{22a} is 2-hydroxyphenyl.

11. A tripodal chelant according to claim 7,
 25 wherein A is N; E¹, E², and E³ are (CH₂)_k-NHCOCH₂N=CH-R^{22a},
 k is 2-3, and R^{22a} is 4-(2-methyl-3-hydroxy-5-
 hydroxymethyl)pyridyl.

12. A tripodal chelant according to claim 5,
 30 wherein A is -[N(L)-CH₂CH₂-]₃-; and E¹, E², and E³ are
 chelating arms each independently having the formula:



13. A tripodal chelant according to claim 12,
 5 wherein A is $-\text{[N(L)-CH}_2\text{CH}_2-]_3-$; E¹, E², and E³ are
 chelating arms each independently having the formula:



10 wherein R²¹ and R²² are independently selected from
 the group consisting of CH_2COOH , and $\text{CH}_2\text{PO(OH)}_2$.

14. A tripodal chelant according to claim 13,
 wherein A is $-\text{[N(L)-CH}_2\text{CH}_2-]_3-$; and E¹, E², and E³ are
 15 $\text{COCH}_2\text{N}(\text{CH}_2\text{COOH})_2$.

15. A radiopharmaceutical compound comprising a
 polypodal chelant according to claim 1, chelated with a
 radionuclide selected from the group consisting of ^{52m}Mn,
 20 ⁵²Fe, ⁵⁵Co, ⁶⁴Cu, ⁶⁷Cu, ⁶⁷Ga, ⁶⁸Ga, ⁹⁰Y, ^{94m}Tc, ^{99m}Tc, ¹⁰⁵Rh, ¹⁰⁹Pd,
¹¹¹In, ^{117m}Sn, ¹⁴⁹Pr, ¹⁵³Sm, ¹⁵⁹Gd, ¹⁶⁶Ho, ¹⁶⁹Yb, ¹⁷⁷Lu, ¹⁸⁶Re, ¹⁸⁸Re,
²⁰³Pb, ²¹¹Pb, and ²¹²Bi.

16. The radiopharmaceutical compound according to
 25 claim 15, wherein said polypodal chelant is
 characterized by having four chelating arms.

17. The radiopharmaceutical compound according to
 claim 15, wherein said polypodal chelant is
 30 characterized by being tripodal.

18. The radiopharmaceutical compound according to claim 17, wherein A of said tripodal chelant is a spacer selected from the group consisting of R^1-C , N , P , $P(O)$, and

5 $-[N(L)C(W)(CR^5R^6)_c]_d-$; R^1 , R^5 , and R^6 are selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkenyl, C_3-C_6 cycloalkyl, benzyl, and phenyl; E^1 , E^2 , and E^3 are chelating arms each independently having the formula:

10



R^{21} and R^{22} are independently selected at each occurrence from the group consisting of H, C_1-C_{10} alkyl 15 substituted with 0-2 R^{23} , C_2-C_{10} alkenyl substituted with 0-2 R^{23} , aryl substituted with 0-2 R^{23} , and C_7-C_{16} alkaryl, wherein the aryl is substituted with 0-2 R^{23} , or R^{21} and R^{22} may be taken together to form a $=CH-R^{22a}$ group, wherein R^{22a} is aryl substituted with 0-5 R^{23} , or 20 heterocycle substituted by 0-5 R^{23} ;

R^{23} is selected from the group consisting of H, OH, C_1-C_3 alkyl, C_1-C_3 hydroxyalkyl, $C(=O)R^{24}$, $C(=O)OR^{24}$, $C(=O)NR^{24}_2$, $PO(OR^{24})_2$ and $S(O)_2OR^{24}$; and

25 R^{24} is selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 fluoroalkyl, C_1-C_6 alkenyl, C_3-C_6 cycloalkyl, benzyl and phenyl.

19. The radiopharmaceutical compound according to claim 18, wherein A is a spacer selected from the 30 group consisting of N , $P(O)$, and $-[N(L)C(W)(CR^5R^6)_c]_d-$; R^5 and R^6 are independently selected at each occurrence from the group consisting of H, C_1-C_6 alkyl, C_3-C_6

cycloalkyl, phenyl and benzyl; E^1 , E^2 , and E^3 are chelating arms each independently having the formula:



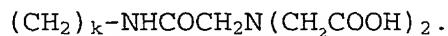
5 wherein R^{21} and R^{22} are independently selected from the group consisting of C_1-C_{10} alkyl substituted with 0-2 R^{23} , and aryl substituted with 0-2 R^{23} , or R^{21} and R^{22} may be taken together to form a $=CH-R^{22a}$ group, wherein R^{22a} is aryl substituted with 0-5 R^{23} , or heterocycle
10 substituted by 0-5 R^{23} ; R^{23} is selected from the group consisting of OH, C_1-C_3 hydroxyalkyl, COOH, $PO(OH)_2$ and $S(O)_2OH$.

15 20. The radiopharmaceutical compound according to claim 19, wherein A is N or $P(O)$; E^1 , E^2 and E^3 are chelating arms each independently having the formula:



20 wherein k is 2-3; R^{21} is independently selected from the group consisting of CH_3 , CH_2COOH , and $CH_2PO(OH)_2$; and R^{22} is independently selected from the group consisting of CH_2COOH , and $CH_2PO(OH)_2$.

25 21. The radiopharmaceutical compound according to claim 20, wherein A is N or $P(O)$; k is 2-3; and E^1 , E^2 and E^3 are



30 22. The radiopharmaceutical compound according to claim 21, wherein A is N; E^1 , E^2 and E^3 are $(CH_2)_k-NHCOCH_2N(CH_2COOH)_2$, and k is 2-3.

23. The radiopharmaceutical compound according to claim 21, wherein A is N; k is 2-3; and E¹, E² and E³ are (CH₂)_k-
5 NHCOCH₂N(CH₃) (CH₂COOH).

24. The radiopharmaceutical compound according to claim 21, wherein A is N; E¹, E² and E³ are (CH₂)_k-
NHCOCH₂N=CH-R^{22a}, k is 2-3, and R^{22a} is 2-hydroxyphenyl.

10

25. The radiopharmaceutical compound according to claim 21, wherein A is N; E¹, E² and E³ are (CH₂)_k-
NHCOCH₂N=CH-R^{22a}, k is 2-3, and R^{22a} is 4-(2-methyl-3-
hydroxy-5-hydroxymethyl)pyridyl.

15

26. The radiopharmaceutical compound according to claim 19, wherein A is -[N(L)-CH₂CH₂-]₃-; and E¹, E² and E³ are chelating arms each independently having the formula:

20

COCH₂NR²¹R²².

27. An MRI contrast agent comprising a polypodal chelant according to claim 1, chelated with a paramagnetic metal ion of atomic number 21-29, 42-44 or
25 58-70.

28. The MRI contrast agent according to claim 27, wherein said polypodal chelant is characterized by having four chelating arms.

30

29. The MRI contrast agent according to claim 28, wherein said polypodal chelant is characterized by being tripodal.

5 30. The MRI contrast agent according to claim 29, wherein A of said tripodal chelant is a spacer selected from the group consisting of R^1-C , N, P, P(O), and $-\text{[N(L)C(W)(CR}^5\text{R}^6\text{)}_c\text{]d-}$; R^1 , R^5 , and R^6 are selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkenyl, C_3-C_6 cycloalkyl, benzyl, and phenyl; E^1 , E^2 , and E^3 are chelating arms each independently having the formula:



15

R^{21} and R^{22} are independently selected at each occurrence from the group consisting of H, C_1-C_{10} alkyl substituted with 0-2 R^{23} , C_2-C_{10} alkenyl substituted with 0-2 R^{23} , aryl substituted with 0-2 R^{23} , and C_7-C_{16} alkaryl, wherein the aryl is substituted with 0-2 R^{23} , or R^{21} and R^{22} may be taken together to form a $=CH-R^{22a}$ group, wherein R^{22a} is aryl substituted with 0-5 R^{23} , or heterocycle substituted by 0-5 R^{23} ;

R^{23} is selected from the group consisting of H, OH, C_1-C_3 alkyl, C_1-C_3 hydroxyalkyl, $C(=O)R^{24}$, $C(=O)OR^{24}$, $C(=O)NR^{24}_2$, $PO(OR^{24})_2$ and $S(O)_2OR^{24}$; and

R^{24} is selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 fluoroalkyl, C_1-C_6 alkenyl, C_3-C_6 cycloalkyl, benzyl and phenyl.

30

31. The MRI contrast agent according to claim 30, wherein A is a spacer selected from the group consisting

of N, P(O), and $-[N(L)C(W)(CR^5R^6)_c]_d-$; R⁵ and R⁶ are independently selected at each occurrence from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, phenyl and benzyl; E¹, E², and E³ are chelating arms each 5 independently having the formula:



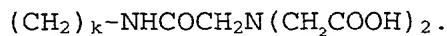
wherein R²¹ and R²² are independently selected from 10 the group consisting of C₁-C₁₀ alkyl substituted with 0-2 R²³, and aryl substituted with 0-2 R²³, or R²¹ and R²² may be taken together to form a =CH-R^{22a} group, wherein R^{22a} 15 is aryl substituted with 0-5 R²³, or heterocycle substituted by 0-5 R²³; R²³ is selected from the group consisting of OH, C₁-C₃ hydroxyalkyl, COOH, PO(OH)₂ and S(O)₂OH.

32. The MRI contrast agent according to claim 31, wherein A is N or P(O); E¹, E² and E³ are chelating arms 20 each independently having the formula:



wherein k is 2-3; R²¹ is independently selected from 25 the group consisting of CH₃, CH₂COOH, and CH₂PO(OH)₂; and R²² is independently selected from the group consisting of CH₂COOH, and CH₂PO(OH)₂.

33. The MRI contrast agent according to claim 32, 30 wherein A is N or P(O); k is 2-3; and E¹, E² and E³ are



34. The MRI contrast agent according to claim 33, wherein A is N; E¹, E² and E³ are (CH₂)_k-NHCOCH₂N(CH₂COOH)₂, and k is 2-3.

5

35. The MRI contrast agent according to claim 33, wherein A is N; k is 2-3; and E¹, E² and E³ are (CH₂)_k-NHCOCH₂N(CH₃)(CH₂COOH).

10 36. The MRI contrast agent according to claim 33, wherein A is N; E¹, E² and E³ are (CH₂)_k-NHCOCH₂N=CH-R^{22a}, k is 2-3, and R^{22a} is 2-hydroxyphenyl.

15 37. The MRI contrast agent according to claim 33, wherein A is N; E¹, E² and E³ are (CH₂)_k-NHCOCH₂N=CH-R^{22a}, k is 2-3, and R^{22a} is 4-(2-methyl-3-hydroxy-5-hydroxymethyl) pyridyl.

20 38. The MRI contrast agent according to claim 31, wherein A is -[N(L)-CH₂CH₂-]₃-; and E¹, E² and E³ are chelating arms each independently having the formula COCH₂NR²¹R²².

25 39. An X-ray or CT contrast agent comprising a polypodal chelant according to claim 1, chelated with a heavy metal ion of atomic number 21-31, 39-50, 56-80, 82, 83 or 90.

30 40. The X-ray or CT contrast agent according to claim 39, wherein said polypodal chelant is characterized by having four chelating arms.

41. The X-ray or CT contrast agent according to claim 40, wherein said polypodal chelant is characterized by being tripodal.

5 42. The X-ray or CT contrast agent according to claim 41, wherein A of said tripodal chelant is a spacer selected from the group consisting of R^1-C , N , P , $P(O)$, and

10 $-[N(L)C(W)(CR^5R^6)_c]_d-$; R^1 , R^5 , and R^6 are selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkenyl, C_3-C_6 cycloalkyl, benzyl, and phenyl; E^1 , E^2 , and E^3 are chelating arms each independently having the formula:

15 $(CH_2)_k-NHCOCH_2NR^{21}R^{22}$

20 R^{21} and R^{22} are independently selected at each occurrence from the group consisting of H, C_1-C_{10} alkyl substituted with 0-2 R^{23} , C_2-C_{10} alkenyl substituted with 0-2 R^{23} , aryl substituted with 0-2 R^{23} , and C_7-C_{16} alkaryl, wherein the aryl is substituted with 0-2 R^{23} , or R^{21} and R^{22} may be taken together to form a $=CH-R^{22a}$ group, wherein R^{22a} is aryl substituted with 0-5 R^{23} , or heterocycle substituted by 0-5 R^{23} ;

25 R^{23} is selected from the group consisting of H, OH, C_1-C_3 alkyl, C_1-C_3 hydroxyalkyl, $C(=O)R^{24}$, $C(=O)OR^{24}$, $C(=O)NR^{24}_2$, $PO(OR^{24})_2$ and $S(O)_2OR^{24}$; and

30 R^{24} is selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 fluoroalkyl, C_1-C_6 alkenyl, C_3-C_6 cycloalkyl, benzyl and phenyl.

43. The X-ray or CT contrast agent according to claim 42, wherein A is a spacer selected from the group consisting of N, P(O), and $-\left[N(L)C(W)(CR^5R^6)_c\right]_d-$; R⁵ and R⁶ are independently selected at each occurrence from 5 the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, phenyl and benzyl; E¹, E², and E³ are chelating arms each independently having the formula:



10

wherein R²¹ and R²² are independently selected from the group consisting of C₁-C₁₀ alkyl substituted with 0-2 R²³, and aryl substituted with 0-2 R²³, or R²¹ and R²² may be taken together to form a =CH-R^{22a} group, wherein R^{22a} 15 is aryl substituted with 0-5 R²³, or heterocycle substituted by 0-5 R²³; R²³ is selected from the group consisting of OH, C₁-C₃ hydroxyalkyl, COOH, PO(OH)₂, and S(O)₂OH.

20

44. The X-ray or CT contrast agent according to claim 43, wherein A is N or P(O); E¹, E² and E³ are chelating arms each independently having the formula:

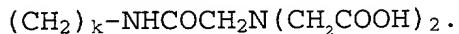


25

wherein k is 2-3; R²¹ is independently selected from the group consisting of CH₃, CH₂COOH, and CH₂PO(OH)₂; and R²² is independently selected from the group consisting of CH₂COOH, and CH₂PO(OH)₂.

30

45. The X-ray or CT contrast agent according to claim 44, wherein A is N or P(O); k is 2-3; and E¹, E² and E³ are



5

46. The X-ray or CT contrast agent according to claim 45, wherein A is N; E¹, E² and E³ are $(\text{CH}_2)_k-\text{NHCOCH}_2\text{N}(\text{CH}_2\text{COOH})_2$, and k is 2-3.

47. The X-ray or CT contrast agent according to claim 45, wherein A is N; k is 2-3; and E¹, E² and E³ are $(\text{CH}_2)_k-\text{NHCOCH}_2\text{N}(\text{CH}_3)(\text{CH}_2\text{COOH})$.

48. The X-ray or CT contrast agent according to claim 45, wherein A is N; E¹, E² and E³ are $(\text{CH}_2)_k-\text{NHCOCH}_2\text{N}=\text{CH}-\text{R}^{22a}$, k is 2-3, and R^{22a} is 2-hydroxyphenyl.

15

49. The X-ray or CT contrast agent according to claim 45, wherein A is N; E¹, E² and E³ are $(\text{CH}_2)_k-\text{NHCOCH}_2\text{N}=\text{CH}-\text{R}^{22a}$, k is 2-3, and R^{22a} is 4-(2-methyl-3-hydroxy-5-hydroxy-methyl)pyridyl.

20

50. The X-ray or CT contrast agent according to claim 43, wherein A is $-\text{[N}(\text{L})-\text{CH}_2\text{CH}_2-]_{,,-}$; and E¹, E² and E³ are chelating arms each independently having the formula:

25



51. A conjugate of the formula:

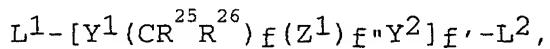
30

BFC-L_n-BM,

and pharmaceutically acceptable salts thereof,

wherein BFC is a polypodal chelant according to claim 1, in which one of R¹ to R²⁴ includes a bond to L_n; L_n is a linking group of formula:

5



L¹ is $[(CH_2)_g Z^1]_{g'} - (CR^{25}R^{26})_{g''} -$;

L² is $-(CR^{25}R^{26})_{g'''} - [Z^1 (CH_2)_g]_{g''} -$;

10 g is independently 0-10;

g' is independently 0-1;

g'' is independently 0-10;

f is independently 0-10;

f' is independently 0-10;

15 f'' is independently 0-1;

Y¹ and Y², at each occurrence, are independently selected from the group consisting of a bond, O, NR²⁶, C=O, C(=O)O, OC(=O)O, C(=O)NH-, C=NR²⁶, S, S(O), S(O)₂, NHC(=O), (NH)₂C(=O) and (NH)₂C=S;

20 R²⁵ and R²⁶ are independently selected at each occurrence from the group consisting of H, C₁-C₁₀ alkyl substituted with 0-5 R²⁷ and alkaryl wherein the aryl is substituted with 0-5 R²⁷;

25 R²⁷ is independently selected at each occurrence from the group consisting of NHR²⁸, C(=O)R²⁸, OC(=O)R²⁸, OC(=O)OR²⁸, C(=O)OR²⁸, C(=O)NR₂²⁸, -CN, SR²⁸, S(O)R²⁸, S(O)₂R²⁸, NHC(=O)R²⁸, NHC(=O)NHR²⁸, NHC(=S)NHR²⁸ and a bond to BM;

R^{28} is independently selected at each occurrence from the group consisting of H, C_1 - C_6 alkyl, benzyl, phenyl and a bond to BM; and

BM is a biologically active molecule selected from
 5 the group consisting of IIb/IIIa receptor ligands, fibrin binding peptides, leukocyte binding peptides, chemotactic peptides, LTB_4 receptor antagonists, somatostatin analogs, selectin binding peptides, vitronectin receptor antagonists, tyrosine kinase
 10 inhibitors, matrix metalloproteinase inhibitors, oligonucleotides, fatty acids, nitroimidazoles, and carbohydrates.

52. A conjugate according to claim 51, wherein
 15 said polypodal chelant is characterized by having four chelating arms.

53. A conjugate according to claim 51, wherein
 20 said polypodal chelant is characterized by being tripodal.

54. A conjugate according to claim 53, wherein A of said tripodal chelant is a spacer selected from the group consisting of R^1 -C, N, P, P(O), and -
 25 $[N(L)C(W)(CR^5R^6)_c]_d$ -; R^1 , R^5 , and R^6 are selected from the group consisting of H, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, C_1 - C_6 alkenyl, C_3 - C_6 cycloalkyl, benzyl, and phenyl; E^1 , E^2 , and E^3 are chelating arms each independently having the formula:

30



R²¹ and R²² are independently selected at each occurrence from the group consisting of H, C₁-C₁₀ alkyl substituted with 0-2 R²³, C₂-C₁₀ alkenyl substituted with 0-2 R²³, aryl substituted with 0-2 R²³, and C₇-C₁₆ 5 alkaryl, wherein the aryl is substituted with 0-2 R²³, or R²¹ and R²² may be taken together to form a =CH-R^{22a} group, wherein R^{22a} is aryl substituted with 0-5 R²³, or heterocycle substituted by 0-5 R²³;

10 R²³ is selected from the group consisting of H, OH, C₁-C₃ alkyl, C₁-C₃ hydroxyalkyl, C(=O)R²⁴, C(=O)OR²⁴, C(=O)NR²⁴₂, PO(OR²⁴)₂ and S(O)₂OR²⁴; and

15 R²⁴ is selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₁-C₆ fluoroalkyl, C₁-C₆ alkenyl, C₃-C₆ cycloalkyl, benzyl and phenyl.

15

55. A conjugate according to claim 54, wherein A is a spacer selected from the group consisting of N, P(O) and -[N(L)C(W)(CR⁵R⁶)_n]_a-; R⁵ and R⁶ are independently selected at each occurrence from the group 20 consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, phenyl and benzyl; E¹, E², and E³ are chelating arms each independently having the formula:



25 wherein R²¹ and R²² are independently selected from the group consisting of C₁-C₁₀ alkyl substituted with 0-2 R²³, and aryl substituted with 0-2 R²³, or R²¹ and R²² may be taken together to form a =CH-R^{22a} group, wherein R^{22a} 30 is aryl substituted with 0-5 R²³, or heterocycle substituted by 0-5 R²³; R²³ is selected from the group consisting of OH, C₁-C₃ hydroxyalkyl, COOH, PO(OH)₂ and S(O)₂OH.

56. A conjugate according to claim 55, wherein A is N or P(O); E¹, E² and E³ are chelating arms each independently having the formula:

5



wherein k is 2-3; R²¹ is independently selected from the group consisting of CH₃, CH₂COOH, and CH₂PO(OH)₂; and R²² is independently selected from the group consisting of CH₂COOH, and CH₂PO(OH)₂.

10

57. A conjugate according to claim 56, wherein A is N or P(O); E¹, E² and E³ are (CH₂)_k-NHCOCH₂N(CH₂COOH)₂, and k is 2-3.

15

58. A conjugate according to claim 57, wherein A is N; E¹, E², and E³ are (CH₂)_k-NHCOCH₂N(CH₂COOH)₂, and k is 2-3.

20

59. A conjugate according to claim 57, wherein A is N; E¹, E², and E³ are (CH₂)_k-NHCOCH₂N(CH₃)(CH₂COOH), and k is 2-3.

25

60. A conjugate according to claim 57, wherein A is N; E¹, E² and E³ are (CH₂)_k-NHCOCH₂N=CH-R^{22a}, k is 2-3, and R^{22a} is 2-hydroxyphenyl.

30

61. A conjugate according to claim 57, wherein A is N; E¹, E² and E³ are (CH₂)_k-NHCOCH₂N=CH-R^{22a}, k is 2-3, and R^{22a} is 4-(2-methyl-3-hydroxy-5-hydroxymethyl)pyridyl.

62. A conjugate according to claim 55, wherein A is $-[N(L)-CH_2CH_2-]_3-$; and E¹, E² and E³ are chelating arms each independently having the formula:

5



63. A radiopharmaceutical compound comprising a conjugate according to claim 51, chelated with a radionuclide selected from the group consisting of ^{52m}Mn, 10 ⁵²Fe, ⁵⁵Co, ⁶⁴Cu, ⁶⁷Cu, ⁶⁷Ga, ⁶⁸Ga, ⁹⁰Y, ^{94m}Tc, ^{99m}Tc, ¹⁰⁵Rh, ¹⁰⁹Pd, ¹¹¹In, ^{117m}Sn, ¹⁴⁹Pr, ¹⁵³Sm, ¹⁵⁹Gd, ¹⁶⁶Ho, ¹⁶⁹Yb, ¹⁷⁷Lu, ¹⁸⁶Re, ¹⁸⁸Re, ²⁰³Pb, ²¹¹Pb, and ²¹²Bi.

64. An MRI contrast agent comprising a conjugate according to claim 51, chelated with a paramagnetic metal ion of atomic number 21-29, 42-44 or 58-70.

65. An X-ray or CT contrast agent comprising a conjugate according to claim 51, chelated with a heavy metal ion of atomic number 21-31, 39-50, 56-80, 82, 83 or 90.

66. A radiopharmaceutical composition for treating pathological processes involving angiogenic neovasculature in a patient in need thereof comprising a therapeutically effective amount of the radiopharmaceutical compound of claim 15 and a pharmaceutically acceptable carrier.

67. The composition of claim 66, wherein said radiopharmaceutical compound comprises a beta, alpha or Auger electron-emitting isotope.

68. A method for treating pathological processes involving angiogenic neovasculature in a patient in need thereof comprising administering to said patient a
5 therapeutically effective amount of the radiopharmaceutical composition of claim 66.

69. A composition for radioactive imaging comprising an effective amount of the
10 radiopharmaceutical compound of claim 15 and a pharmaceutically acceptable carrier.

70. A method for radioactive imaging comprising administering to a patient to be imaged sufficiently in
15 advance thereto an effective amount of the radioactive imaging composition of claim 69.

71. A method according to claim 70, wherein said imaging method is gamma scintigraphy or positron-emission tomography.
20

72. A composition for X-ray imaging comprising an effective amount of the contrast agent of claim 39 and a pharmaceutically acceptable carrier.
25

73. A method for X-ray imaging comprising administering to a patient to be imaged sufficiently in advance thereof an effective amount of the X-ray imaging composition of claim 72.
30

74. A method according to claim 73, wherein said X-ray imaging method is CT imaging.

75. A composition for magnetic resonance imaging 5 comprising an effective amount of the contrast agent of claim 27 and a pharmaceutically acceptable carrier.

76. A method for magnetic resonance imaging comprising administering to a patient to be imaged 10 sufficiently in advance thereof an effective amount of the magnetic resonance imaging composition of claim 75.

77. A pharmaceutical composition for treating heavy metal toxicity in a patient in need thereof, 15 comprising a therapeutically effective amount of the polypodal chelant of claim 1 and a pharmaceutically acceptable carrier.

78. A method for treating heavy metal toxicity in 20 a patient in need thereof, comprising administering to said patient a therapeutically effective amount of the pharmaceutical composition of claim 77.

79. A radiopharmaceutical treatment kit 25 comprising: a sterile, non-pyrogenic formulation comprising a radiopharmaceutical composition according to claim 66, a pH 3-9 buffering agent and optionally one or more additives selected from the group consisting of ancillary ligands, reducing agents, transfer ligands, 30 buffers, lyophilization aids, stabilization aids, solubilization aids, bacteriostats and equipment for administering said composition.

solubilization aids, bacteriostats and equipment for administering said composition.

80. The treatment kit of claim 79, wherein said
5 formulation is in the form of a sterile solution or lyophilized solid.

81. A diagnostic kit comprising: a sterile, non-pyrogenic formulation comprising a radiopharmaceutical composition according to claim 66, a
10 pH 3-9 buffering agent and optionally one or more additives selected from the group consisting of ancillary ligands, reducing agents, transfer ligands, buffers, lyophilization aids, stabilization aids, solubilization aids, bacteriostats and equipment for
15 administering said composition.

82. The diagnostic kit of claim 81, wherein said formulation is in the form of a sterile solution or lyophilized solid.

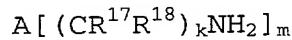
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83. A diagnostic kit comprising: a sterile, non-pyrogenic formulation comprising an X-ray imaging composition according to claim 72, a pH 3-9 buffering agent and optionally one or more additives selected from
25 the group consisting of ancillary ligands, reducing agents, transfer ligands, buffers, lyophilization aids, stabilization aids, solubilization aids, bacteriostats and equipment for administering said composition.

30
84. The diagnostic kit of claim 83, wherein said formulation is in the form of a sterile solution or lyophilized solid.

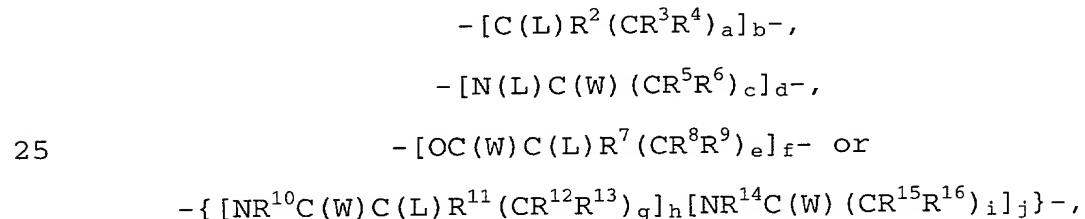
85. A diagnostic kit comprising: a sterile, non-pyrogenic formulation comprising a magnetic resonance imaging composition according to claim 75, a
 5 pH 3-9 buffering agent and optionally one or more additives selected from the group consisting of ancillary ligands, reducing agents, transfer ligands, buffers, lyophilization aids, stabilization aids, solubilization aids, bacteriostats and equipment for
 10 administering said composition.

86. The diagnostic kit of claim 85, wherein said formulation is in the form of a sterile solution or lyophilized solid.

15 87. A compound having the formula:



20 wherein A is a spacer selected from the group consisting of R¹-C, R¹-Si, R¹-Ge, N, P and P(O), or a macrocyclic group having the formula:



wherein a is an integer selected from 1 to 3;
 b is an integer selected from 3 to 5;
 30 c is an integer selected from 1 to 3;
 d is an integer selected from 3 or 4;
 e is an integer selected from 1 to 3;

f is an integer selected from 3 or 4;
 g is an integer selected from 1 to 3;
 h is an integer selected from 3 or 4;
 i is an integer selected from 1 to 3;
 5 j is an integer selected from 0 to 3;
 k is an integer selected from 0 to 3;
 m is an integer selected from 3 or 4;
 L is a direct bond to $[(CR^{17}R^{18})_kNH_2]$;
 W is H₂ or O;
 10 R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³,
 R¹⁴, R¹⁵, and R¹⁶ are independently selected at each
 occurrence from the group consisting of H, C₁-C₆ alkyl,
 C₃-C₆ cycloalkyl, C₁-C₆ fluoroalkyl, C₁-C₆ alkenyl, C₃-C₆
 cycloalkenyl, C₁-C₆ fluoroalkenyl, benzyl, fluorobenzyl,
 15 phenyl and fluorophenyl;
 R¹⁷ and R¹⁸ are independently selected from the
 group consisting of H, C₁-C₁₀ alkyl substituted with 0-5
 R²³,
 C₁-C₁₀ fluoroalkyl substituted with 0-5 R²³, C₂-C₁₀
 20 alkenyl substituted with 0-5 R²³, C₂-C₁₀ fluoroalkenyl
 substituted with 0-5 R²³, aryl substituted with 0-5 R²³,
 C₇-C₁₆ alkaryl wherein the aryl is substituted with 0-5
 R²³, and fluoroaryl substituted with 0-5 R²³; or R¹⁷ and
 R¹⁸ may be taken together to form a C₃-C₁₀ cycloalkyl or
 25 C₃-C₁₀ cycloalkenyl optionally interrupted with C(O)NH,
 NH, NHC(O), NHC(O)NH, NHC(S)NH, O, S, S(O), S(O)₂,
 P(O)(OR²⁴), P(O)(OR²⁴)O or P(O)(NHR²⁴)O, or to form a =CH-
 R^{22a} group, wherein R^{22a} is aryl substituted with 0-5 R²³
 or heterocycle substituted by 0-5 R²³;
 30 R²³ is selected from the group consisting of H, OH,
 C₁-C₃ alkyl, C₁-C₃ hydroxyalkyl, C(=O)R²⁴, C(=O)OR²⁴,
 C(=O)NR²⁴₂, PO(OR²⁴)₂ and S(O)₂OR²⁴; and

R^{24} is selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, C₁-C₆ fluoroalkyl, C₁-C₆ alkenyl, C₃-C₆ cycloalkyl, C₁-C₆ fluoroalkenyl, benzyl, fluorobenzyl, phenyl, and fluorophenyl.

5

88. A compound according to claim 60, wherein m is 4.

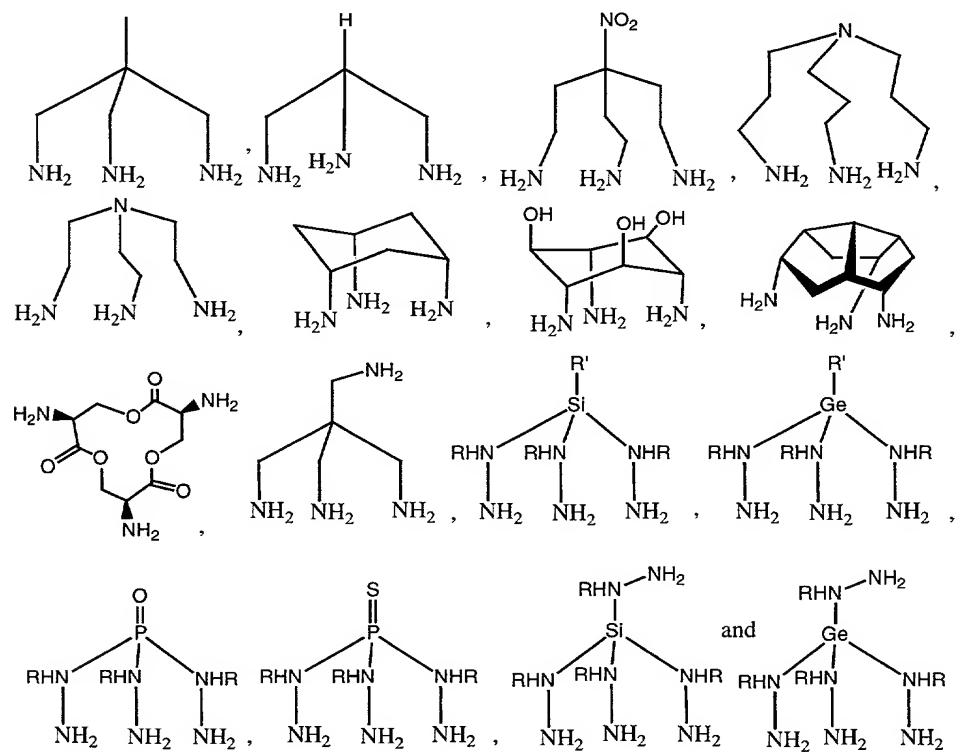
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89. A compound according to claim 60, wherein m is 3.

90. A compound according to claim 62, wherein A is N or -[N(L)-C₂H₅]₃-; k is 0, 2 or 3; and R¹⁷ and R¹⁸ are H.

15

91. A compound according to claim 89, which is selected from the group consisting of:



92. A radiopharmaceutical composition for treating pathological processes involving angiogenic neovasculature in a patient in need thereof comprising a therapeutically effective amount of the
5 radiopharmaceutical compound of claim 63 and a pharmaceutically acceptable carrier.

93. The composition of claim 92, wherein said radiopharmaceutical compound comprises a beta, alpha or
10 Auger electron-emitting isotope.

94. A method for treating pathological processes involving angiogenic neovasculature in a patient in need thereof comprising administering to said patient a
15 therapeutically effective amount of the radiopharmaceutical composition of claim 92.

95. A composition for radioactive imaging comprising an effective amount of the
20 radiopharmaceutical compound of claim 63 and a pharmaceutically acceptable carrier.

96. A method for radioactive imaging comprising administering to a patient to be imaged sufficiently in
25 advance thereto an effective amount of the radioactive imaging composition of claim 95.

97. A method according to claim 96, wherein said imaging method is gamma scintigraphy or positron-
30 emission tomography.

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98. A composition for X-ray imaging comprising an effective amount of the contrast agent of claim 65 and a pharmaceutically acceptable carrier.

5 99. A method for X-ray imaging comprising administering to a patient to be imaged sufficiently in advance thereof an effective amount of the X-ray imaging composition of claim 98.

10 100. A method according to claim 99, wherein said X-ray imaging method is CT imaging.

15 101. A composition for magnetic resonance imaging comprising an effective amount of the contrast agent of claim 64 and a pharmaceutically acceptable carrier.

20 102. A method for magnetic resonance imaging comprising administering to a patient to be imaged sufficiently in advance thereof an effective amount of the magnetic resonance imaging composition of claim 101.

103. A radiopharmaceutical treatment kit comprising: a sterile, non-pyrogenic formulation comprising a radiopharmaceutical composition according 25 to claim 92, a pH 3-9 buffering agent and optionally one or more additives selected from the group consisting of ancillary ligands, reducing agents, transfer ligands, buffers, lyophilization aids, stabilization aids, solubilization aids, bacteriostats and equipment for 30 administering said composition.

104. The treatment kit of claim 103, wherein said formulation is in the form of a sterile solution or lyophilized solid.

5 105. A diagnostic kit comprising: a sterile, non-pyrogenic formulation comprising a radiopharmaceutical composition according to claim 92, a pH 3-9 buffering agent and optionally one or more additives selected from the group consisting of
10 ancillary ligands, reducing agents, transfer ligands, buffers, lyophilization aids, stabilization aids, solubilization aids, bacteriostats and equipment for administering said composition.

15 106. The diagnostic kit of claim 105, wherein said formulation is in the form of a sterile solution or lyophilized solid.

20 107. A diagnostic kit comprising: a sterile, non-pyrogenic formulation comprising an X-ray imaging composition according to claim 98, a pH 3-9 buffering agent and optionally one or more additives selected from the group consisting of ancillary ligands, reducing agents, transfer ligands, buffers, lyophilization aids,
25 stabilization aids, solubilization aids, bacteriostats and equipment for administering said composition.

30 108. The diagnostic kit of claim 107, wherein said formulation is in the form of a sterile solution or lyophilized solid.

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109. A diagnostic kit comprising: a sterile, non-pyrogenic formulation comprising a magnetic resonance imaging composition according to claim 101, a pH 3-9 buffering agent and optionally one or more 5 additives selected from the group consisting of ancillary ligands, reducing agents, transfer ligands, buffers, lyophilization aids, stabilization aids, solubilization aids, bacteriostats and equipment for administering said composition.

10

110. The diagnostic kit of claim 109, wherein said formulation is in the form of a sterile solution or lyophilized solid.

15